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842-5 Coronary Ultrasound Thrombolysis In Acute Myocardial Infarction: Results From the ACUTE Study

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Background: Clinical data suggest that therapeutic ultrasound selectively ablates thrombi with wide margins of safety. The purpose of the ACUTE study is to evaluate the safety and efficacy of percutaneous coronary ultrasound thrombolysis (CUT) as the primary reperfusion therapy in acute anterior myocardial infarction (AMI) in a multicenter study.

Methods: Patients (pts) with AMI and occluded left anterior descending artery were treated by CUT using a novel percutaneous therapeutic ultrasound device.

Results: CUT was attempted in 31 consecutive pts. Sonication (45 kHz, 18W, ≤3 min) induced arterial patency in 29 (94% of the pts), (TIMI 3 flow in 84%), and residual stenosis of 54 ± 26%. There were no dissections, perforations, embolization, spasm or "no-reflow". There were no adverse clinical events during CUT. Adjunct PTCA resulted in residual stenosis of 17 ± 15%. Stents were deployed in 7 pts (22%). There was no adjunct use of thrombolytic drugs. Reopro was administered in 1 pt (3%). In-hospital, 1 pt (3%) developed reinfarction, and 3 pts (10%) had recurrent ischemia with a need for urgent target vessel revascularization. Six pts (19%) had CHF (NYHC ≥III). There were no deaths, stroke, bleeding or need for vascular repair.

Conclusion: CUT is potentially a safe and effective device-solution for reperfusion therapy in the setting of AMI.

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842-6 Critical Pathway for Acute ST Segment Elevation Myocardial Infarction: Evaluation of the Potential Impact in the TIMI 9 Registry

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Physicians are under increasing pressure to reduce costs and maintain high quality of care. Critical pathways may help accomplish this goal. We designed a critical pathway for acute MI which targets 100% use of appropriate medications (i.e., thrombolysis [or primary angioplasty], aspirin, heparin, beta-blockers, ACE inhibitors) and incorporates a strategy of early hospital discharge (day 4) for low-risk patients. Cardiac catheterization is recommended only for ACC/AHA-recommended indications (recurrent ischemia, low ejection fraction, or other complication). We evaluated the potential impact of this critical pathway using the TIMI 9 Registry database, where 840 consecutive patients with acute ST elevation MI were enrolled at 20 hospitals in the U.S. and Canada. Thrombolysis was used in 503 (60%), primary angioplasty in 77 (9%) and no reperfusion therapy in 31%. Only 87% of pts. received aspirin. Of those with documented LV dysfunction or congestive failure, 39% were treated with ACE inhibitors, indicating that use of a critical pathway targeting 100% use of these medications would improve care. To evaluate the potential economic impact of the critical pathway on low-risk patients, 141 of 503 thrombolysis patients had no recurrent ischemia or MI, shock, CHF through discharge. Their mean length of stay was 8.2 ± 5.4 days, with 88% staying in-hospital ≤than the target of 4 days. Of these uncomplicated patients, 110 had preserved LV function, yet 64% underwent catheterization and 33% underwent PTCA. For the 77 primary angioplasty patients, 38 had no complications, and their mean length of stay was 7.0 ± 3.0 days, with 90% staying ≤4 days. If the critical pathway were used for these low-risk patients (assuming costs of $1000/hospital day, $2000/cath, $3500/PTCA), over $500,000 could be saved for every 100 uncomplicated thrombolysis patients, and $350,000 for every 100 uncomplicated PTCA patients.

Conclusions: 1) These findings from the TIMI 9 Registry demonstrate that significant opportunities exist for improving the medical management of patients with acute MI. 2) Critical pathways may help reduce costs while preserving (or improving) quality of care.

TUESDAY ORAL

843 Aspects of the Congenital Long QT Syndrome

Tuesday, March 31, 1998, 10:30 a.m.–Noon
Georgia World Congress Center, Room 256W

10:30

843-1 Long QT Genotype Can Be Identified by ECG Phenotype

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Background: In a previous study we (Moss, et al) described different ECG T-wave patterns in the LQT1, 2 and 3 genotypes. In this study, we assessed the diagnostic sensitivity/specificity of the Moss patterns and formulated an enhanced criteria set based on new observations.

Methods: Two hundred 12-lead ECGs representing LQT1 (n = 55), LQT2 (79), LQT3 (27), and unaffected (39) genotyped patients (all non-medicated) were read by blinded LQTS researchers. The ECGs were classified as having a LQT1, LQT2, LQT3, unaffected, or an uncertain phenotype using Moss pattern: ST-T morphology, T wave amplitude and duration. The ECG's were also classified using Moss pattern plus new criteria: ST length and slope; distinctiveness of T wave onset/offset, and T wave symmetry. In an expanded set of LQT1 (n = 88), LQT2 (103), and LQT3 (32) records we evaluated age dependent patterns.

Results:

	Sensitivity				Specificity			
Genotype	LQT1	LQT2	LQT3	NL	LQT1	LQT2	LQT3	NL
Moss	0.22	0.30	0.56	0.92	0.97	0.93	0.97	0.78
New Criteria	0.87	0.85	0.70	0.85	0.87	0.94	0.99	0.97

A new phenotype is described in LQT1 patients: short ST segment, asymmetrical peaked T wave, and no clear T onset. (See Example) This new phenotype was expressed by 70% of LQT1 children 0–5 yrs, 6% of older LQT1 children and adults, 0% of LQT2 children, 2% of LQT2 adults, and 0% of all LQT3 patients.

Conclusion: Sensitivity was low in identifying LQT1 and LQT2 using Moss patterns. Sensitivity increased significantly for LQT1 and LQT2 using new phenotypic criteria. In children <6 yrs, using new criteria is essential for LQT1 genotype identification.

10:45

843-2 Wavelet Analysis of Short-term Beat-to-Beat Variability of Repolarization in LQTS Patients With SCN5A Sodium Channel Mutation

J.P. Couderc, W. Zareba, A.J. Moss. *Univ. of Rochester, NY, USA*

Current techniques evaluating beat-to-beat variability of repolarization rely on accurate determination of T-wave endpoints. This study proposes a method to detect a very short-term repolarization variability in a standard 12-lead ECG using the wavelet transformation (WT) technique.

Methods: Using wavelets from the second gaussian derivative, we filtered the repolarization segment to evaluate variability in 10 LQTS pts with SCN5A mutation (SCN5A+), 13 nonlinked family members (SCN5A−), and 28 unrelated healthy subjects (N). From 10-second ECGs, segments beginning 100 ms after the R peak and ending 220 ms before the following R peak were analyzed. Two parameters quantified beat-to-beat changes of the repolarization segment: the temporal variability in time (TVT) and in amplitude (TVA). Mean value of TVT and TVA from the 12 leads were computed and compared to the mean value of the standard deviation of RT apex duration (SDRTm), a time-domain measure of variability.

Results: Comparison of TVA, TVT, their combination, and SDRTm is shown in the Table (* $p < 0.01$, ** $p < 0.00001$ in reference to group N).

	N (n = 28)	SCN5A− (n = 13)	SCN5A+ (n = 10)
SDRTm (ms)	8 ± 6	14 ± 21	31 ± 41*
SDRTm >21 ms	4%	0%	40%
TVA (°)	12 ± 6	19 ± 9	29 ± 17**
TVT (ms)	4 ± 2	5 ± 3	15 ± 17*
(1) TVA >24°	7%	23%	50%
(2) TVT >2.1 ms	4%	14%	50%
(1) or (2)	11%	30%	90%

Conclusions: 1) SCN5A+ pts have increased beat-to-beat repolarization variability. 2) WT provides insight into time and amplitude of T-wave variability without the need to identify T wave endpoints. 3) The combination of wavelet time and amplitude variability parameters provided very effective phenotypic identification of SCN5A+ pts.

11:00

843-3 Prevalence of the Bifid T Waves in Genotyped LQTS Children

L. Zhang, K.W. Timothy, J. Fox, M.H. Lehmann, K.J. Meyer, A.J. Moss, J.L. Robinson, P.J. Schwartz, M.T. Keating, J.A. Towbin, G.M. Vincent. *LDS Hospital, University of Utah, Salt Lake City, UT, USA*

Background: Our group previously reported that LQTS children had more bifid (obvious or subtle) T waves (BI-T) on 12-lead ECGs than normal children (NL). In this study we determined the frequency of BI-T by specific genotype in both younger and older children.

Methods: ECGs of 99 LQTS (58 LQT1, 26 LQT2, 15 LQT3), and 462 NL, all unmedicated, age range 0–15 yrs, were studied. Some patients had multiple ECGs at different ages, yielding 199 LQTS and 623 NL records for this study. The frequency of BI-T in 12 leads was compared for the three genotypes and NL in two age groups (0–5 yrs and 6–15 yrs) using Wilcoxon Matched-Pairs Signed-Ranks test.

Results:

	0–5 yrs				6–15 yrs			
	NL	LQT1	LQT2	LQT3	NL	LQT1	LQT2	LQT3
BI-T%*	18.5	45	63	2.1	8.6	14	64.8	4.8
p**		0.0022	0.0047	0.0076		0.0653†	0.0029	0.0995

* average of all 12 leads ** each genotype compared with NL † obvious plus subtle BI-T; for subtle BI-T alone, p = 0.0029

The frequencies of BI-T within genotypes were significantly different: LQT2 >LQT1 >LQT3 (p values not shown) in both age groups. In LQT1, the frequency of BI-T also varied by age, with a lower % in older children (p = 0.0022).

Conclusions: LQT1 and LQT2 children have significantly more BI-T than do NL. The frequency of BI-T in LQTS children is different by genotype with the highest in LQT2 and lowest in LQT3. The frequency decreases with increasing age in LQT1, whereas it remains unchanged in LQT2. These findings may increase understanding of LQTS genotype pathophysiology, and may be helpful for clinical diagnosis.

11:15

843-4 A Mutation in KVLQT1 Causes Decreased Sinus Rate Without Evidence of Autonomic Nervous Abnormalities

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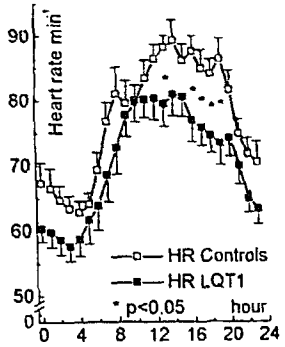
Background: We previously demonstrated abnormally low maximal heart rate during maximal exercise test in long QT syndrome type 1 (LQT1) patients. We therefore investigated whether a sinus node impairment is also present at lower heart rates and whether it is associated with altered autonomic nervous activity.

Methods: Circadian rhythmicity of heart rate (HR) and heart rate variation (HRV) were assessed in 19 LQT1 patients with Asp188Asn mutation of KVLQT1 gene (LQT1) and 19 healthy controls (C) matched for age (LQT1: 41 ± 19, C: 39 ± 19 years) and gender (7 men, 12 women in each group). All subjects underwent 24-hour Holter recording in sinus rhythm without medications.



	LQT1	C	p-value
HR	70 ± 10	76 ± 8	<0.05
SDANN	144 ± 45	136 ± 31	NS
HF	14 ± 7	16 ± 10	NS
LF	23 ± 10	27 ± 9	NS
LF/HF	1.7 ± 0.4	1.9 ± 0.5	NS

Results: HR was lower in LQT1 (table and fig.). No differences were found in HRV variables (table).

Conclusions: Sinus rate was found lower than normal even during rest and regular daily activities. The decreased rate could not be attributed to any alteration in autonomic nervous function. These results suggest that a potassium channel defect in KVLQT1 is responsible for the decreased sinus rate.

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843-5 ECG Repolarization Parameters in LQTS Family Members With Borderline QTc Duration and Cardiac Events

W. Zareba, A.J. Moss, J. Robinson, M. Andrews, P.J. Schwartz, G.M. Vincent, S.G. Priori, J. Benhorin, E.H. Locati, J.A. Towbin, M.H. Lehmann, W.J. Hall, C. Napolitano, L. Zhang, K. Timothy. *University of Rochester, Rochester, NY, USA*

QTc duration of 0.42–0.47 sec can be found in both linked and non-linked LQTS pts. The aim of the study was to evaluate an association between clinical and ECG variables with cardiac events (CE) in 2,008 family members of LQTS pts with borderline QTc (0.42–0.47) enrolled in the International LQTS Regstry. Results of CE and noCE groups as follows:

Variables	no CE (n = 1,715)	CE (n = 293)	
Median Age at ECG (yrs)		28	29
Females		946 (55%)	197 (67%)*
Mean RR (ms)		787 ± 191	864 ± 212*
Age-adjusted bradycardia		267 (16%)	77 (26%)*
QTc (ms)		436 ± 18	446 ± 21*
QTmc (ms)		341 ± 27	353 ± 29*
TmTpc (ms)		95 ± 24	93 ± 23
L2 T wave: flat	112 (7%)	23 (8%)	
broad	40 (2%)	7 (2%)	
bifid biphasic	42 (2%)	7 (2%)	

* p < 0.001

Conclusions: In LQTS family members with borderline QTc duration, a longer QTc duration, bradycardia, and female gender are associated with increased likelihood of cardiac events. Morphologic T-wave abnormalities are infrequent and do not have prognostic significance in LQTS family members with borderline QTc.

11:45

843-6 Non-stationarity of Microvolt T Wave Alternans in Long QT Syndrome Patients

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Background: Detection of microvolt T wave alternans (TWA) is a non-invasive method to identify pts at risk for sudden cardiac death. ECG tracings with visible TWA often show non-stationary pattern of this phenomenon. The purpose of the study was to evaluate stationarity of TWA in long QT syndrome (LQTS) pts, using our new correlation method (CM) for microvolt TWA detection.

Method and Results: Differently from accepted spectral method (SM), CM is able to identify TWA in as few as seven beats, and to detect which beats are alternating. In a group of 32 LQTS pts, 128-beat ECG recordings were performed to detect TWA using both CM and SM. TWA was identified by CM in 14 (44%) pts, and in 4 (13%) pts using SM. The features of TWA detected by CM in relation to the number of alternating beats (N) are shown in the following table (A_{CM} = alternans correlation amplitude; NS_TWA = non-stationary TWA; SNS_TWA = strongly NS_TWA; S_TWA = stationary TWA).

	SNS_TWA N < 38	NS_TWA 38 ≤ N ≤ 64	S_TWA N >64	p**
#pts	8	4	2	
N	20 ± 9	45 ± 10	78 ± 15	
A_{CM} (μV)	83 ± 51	35 ± 14*	44 ± 5*	0.094
RR (ms)	957 ± 203	1115 ± 55*	1264 ± 22	0.061

* p < 0.05 when comparing SNS_TWA vs. NS_TWA and S_TWA. ** Kruskall-Wallis Test

Significant correlations between A_{CM} and RR (r = 0.70; p = 0.005) and between N and RR (r = −0.57; p = 0.033) were observed.